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HL

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY	DOCKET NO.
09/115,963	07/15/98	SCHNEIDER	M	1201-52

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EXAMINER
HOLLINDEN, G

ART UNIT	PAPER NUMBER
1616	

DATE MAILED:

8
09/29/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/115,963	Applicant(s) Schneider et al
	Examiner Gary E. Hollinden	Group Art Unit 1616

☒ Responsive to communication(s) filed on 7/15/98; 4/23/99

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-7 and 13-48 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-7 and 13-48 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☒ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☒ received.

☐ received in Application No. (Series Code/Serial Number) _____

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: EP 93810885.9

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Claims 1-7 and 13-48 have been presented for examination and will be reviewed on their merits. The preliminary amendment, filed July 15, 1998, wherein claims 8-12 were canceled, claims 15-48 were added, and claims 1, 2, and 13 were amended, was entered prior to this examination on the merits.

Administrative Notice

Administrative notice is taken that the terms microbubbles, microballoons, microparticles, microspheres, gas bubbles, microcapsules, gas filled liposomes, etc. have been used so interchangeably in the ultrasound arts as to render them indistinguishable from one another. While subtle nuances have been recognized, the distinctions cannot be clearly defined and so, at best, the terms clearly overlap. It is incumbent upon the PTO that "during patent examination, claims must be interpreted as broadly as they reasonably allow, in order to achieve complete exploration of applicant's invention and its relationship to prior art, so that ambiguities can be recognized, scope and breadth of language explored, and clarification imposed"¹ Thus, for example, the recitation of a microsphere in the instant claim designated invention would not automatically be considered to be patentably distinct from a prior art reference which taught a microballoon. Rather, the patentability determination would hinge on the particular materials being used in each.

Effective Priority Date

It is noted that the effective priority date of the instant claims still appears to be January 23, 1992 - the priority date of previously claimed EP 92810046. The other priority documents now recited do not appear to disclose the specific gases claimed and, as such, do not convey the instant claimed invention.

In addition, it is noted that Patentee has not perfected priority to all of the foreign priority cases which are now being claimed. Patentee did not perfect priority to EP 93810885.9 in the original patent of which this application is a

¹*In re Zletz*, 13 USPQ2d 1320, CA FC 1989; *In re Prater*, 162 USPQ 541, CCPA 1969.

reissue nor does it appear that a claim for priority to said EP document was perfected in any of the US applications now claimed.

§ 102 Rejection

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

"A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States."

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent."

Claims 1, 12-17, 32-36, 42 and 48 are rejected under 35 U.S.C. § 102(b,e) as being anticipated by Albayrak (5,730,954; PTO-892 dated 9/24/99).

These claims appear to be directed towards a composition comprising a suspension containing surfactants and microbubbles of one of several halogenated hydrocarbon gas species (including SF₆).

Albayrak et al. teach several poorly soluble gases including SF₆ and further teach that said gases would be formed in an albumin containing solution. Administrative notice is taken that the albumin in the solution would be fully expected to assemble at the air liquid interface.

Therefore, those claims which would encompass an ultrasonic composition comprising microbubbles of SF₆, surrounded by an interface membrane which would include albumin are anticipated.

§ 103 Rejection

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a

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whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 1-7 and 13-48 are rejected under 35 U.S.C. § 103 as being unpatentable over Rössling et al. (5,501,863; Protest filed 4/23/99), Tickner '251 (Protest filed 4/23/99), Tickner et al. '885 (C; Protest filed 4/23/99), Illum (PTO-892 dated 9/24/99), Albayrak (5,730,954; PTO-892 dated 9/24/99) Glajch et al. (5,147,631; PTO-892 dated 9/24/99), Swanson (PTO-892 dated 9/24/99), and Hilmann et al. (4,466,442; Protest filed 4/23/99) in view of Lincoff et al. (PTO-892 dated 9/24/99), Lincoff et al. (PTO-892 dated 9/24/99), Gardner et al. (PTO-892 dated 9/24/99) Jacobs (PTO-892 dated 9/24/99) and the Dupont Technical Bulletin (PTO-892 dated 9/24/99).

These claims appear to be directed towards a composition comprising a suspension containing surfactants and microbubbles of a halogenated hydrocarbon gas which is poorly soluble in water.

Each of Rössling et al. Tickner '251, Tickner et al. '885, Glajch et al., Swanson, Ryan et al. and Hilmann et al. teach various types of gas filled microspheres. Each of Rössling et al. Tickner '251, Tickner et al. '885, Glajch et al., Swanson further teach that fluorinated gases may be used. Rössling et al. specifically teach as potential gases both sulfur hexafluoride and a low molecular weight fluorinated hydrocarbon, both of which are poorly soluble in water. Tickner and Tickner et al., teach microbubbles enclosed in various interfacial membranes along with a genus of fluorinated gases; namely Freon[®]. The term Freon[®] actually represents a well defined class of small halogen containing molecules. The Dupont Technical Bulletin teaches that fluorinated molecules are a well known and explicitly exemplified sub-group of the compounds encompassed by the term Freon[®]. In particular, the claim designated perfluoroethane, perfluoropropane, and perfluorocyclobutane are Freons[®] (Freon[®]-116, Freon[®]-218 and Freon[®]-318, respectively). Consequently, when taken with the Dupont Technical bulletin, the

disclosures of Tickner and Tickner et al. clearly teach fluorinated chemicals. Illum et al. (page 5; examples 2 and 4-8) teach the formation of microbubbles using poorly soluble volatile gases and further teach that the gas inside the microbubbles would be a mixture of air and the volatile gas. Swanson et al. particularly teach perfluorocarbons that are gases at 37° C². Albayrak et al. teach several poorly soluble gases including SF₆ and further teach that said gases would be formed in an albumin containing solution. Administrative notice is taken that the albumin in the solution would be fully expected to assemble at the air liquid interface. Glajch et al. (col. 6, lines 58-66) specifically teach the use of the claim designated perfluoromethane and perfluoroethane as well as other insoluble gases such as helium and argon. Lincoff et al., Lincoff et al., Gardner et al. and Jacobs teach the desirability of using small perfluorocarbon molecules in vivo because of the stability, safety, acceptable acoustic properties. In addition, the Lincoff publications specifically teach perfluoroethane, perfluoropropane, and perfluorobutane and Jacobs specifically teaches SF₆.

Since each of Rössling et al., Swanson, Tickner, Tickner et al., Albayrak et al., Glajch et al. Swanson et al. Ryan et al. and Hilmann et al. teach that their microbubble compositions would be useful for ultrasonic imaging, all of them may be considered to be in the same field of endeavor. While the Lincoff et al. publications and Gardner et al. are not directed towards ultrasonic imaging and thus could not be considered to be within the same field of endeavor as the references cited above, they specifically address the importance and the usefulness of small perfluorocarbon gases in vivo; giving particular attention to the long persistence of their effect due to their insolubility. Thus, they are pertinent to the problem that inventors in the ultrasonic imaging arts were trying to solve at the time of the invention. Tickner et al. (col. 4, lines 16-29) and Rössling et al. specifically address the importance of finding a gas which has a long duration in the blood and note low solubility as a criteria. In addition, Jacobs serves as a bridge between the ultrasonic imaging arts and the therapeutic art in that Jacobs also is primarily concerned with the therapeutic uses of the perfluorocarbon gases

²Which would include C₁F₄ - C₅F₁₂.

yet also teaches that ultrasonic imaging techniques may be applied to bubbles of perfluorocarbon gases. While the type of large bubble ultrasonic imaging used by Jacobs is not the same as microbubble imaging, it still serves as a bridge in that a person of ordinary skill, while searching through the ultrasonic imaging literature, would find a cross reference to Jacobs and thus find further information about the duration problem they were attempting to solve. It is also important to note that Lincoff et al., Lincoff et al., Gardner et al. and Jacobs teach that small fluorinated molecules are safe in quantities that are orders of magnitude beyond the quantities injected in a bolus of microbubbles. This is also a problem that would be extremely pertinent when determining what gas to use in *in vivo* ultrasonic imaging.

While the prior art references fail to particularly teach each and every gas that would be poorly soluble, it would have been obvious to those of ordinary skill in the art that essentially any poorly soluble gas could be used because the prior art references teach that a large and representative list of poorly soluble gases are useful for ultrasonic imaging. One of ordinary skill would have been motivated to particularly select poorly soluble molecules from among the possible gases to be used in each of Rössling et al. Tickner '251, Tickner et al. '885, Glajch et al., Swanson and Albayrak et al. because Lincoff et al., Lincoff et al., Gardner et al. and Jacobs teach the desirability of using poorly soluble gases in *in vivo* ultrasonic applications

The claimed subject matter fails to patentably distinguish over the state of the art as represented by the cited references. Therefore, the claims are properly rejected under 35 U.S.C. § 103.

Conclusion

In view of the objections /rejections to the pending claims set forth above, no claims may be allowed at this time.

It is noted that certain claims were indicated as patentable by the protester. However, said claims cannot yet be allowed in the instant application for the following reasons:

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1) All of the claims indicated as being allowable are dependent claims which are based on a rejected independent claim.

2) The claims were indicated as being allowable on the basis of experiments performed by the protester. The data contained therein does not appear to have been published. Since it is not published, the propriety of considering unexpected results data from a source other than Patentee is not clear.

The processing of this application can be expedited by providing the following information or changes in your next amendment:

- Proper cross-reference to related applications for which priority is claimed under 35 U.S.C. § 120 in the first paragraph of the specification - including current status (M.P.E.P. 201.11)
- Early filing of an Information Disclosure Statement that includes a PTO-1449 form wherein the document number, publication date, inventor, country of publication, and US patent classification is listed for each patent document and wherein the author, title, journal, volume, issue (if known), pages, and year of publication is listed for all journal references (M.P.E.P. 609). A timely prior art disclosure by the Applicant aids in a speedy prosecution and helps to insure that the patent granted is both valid and enforceable.
- A descriptive title (M.P.E.P. 606 and 606.01). Please note that 1-2 word titles are generally unacceptable.
- Ensuring that each of the drawings presented (if any) are described in the brief description of the drawings. Please note that if a drawing has more than one figure in it (e.g. Figures 1A and 1B), each of the figures must be individually described.
- An abstract which is descriptive of the disclosed invention and contains the chemical structure of the active ingredient(s).
- Correction of any ambiguities in the specification which may lead to a printer inquiry, such as blank spaces which appear to be omissions.
- Correction of any typographical errors in the application.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to the Group 1600 fax machine at 703/308-4556. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30; November 15 1989.

Any inquiry concerning this Office Action or any earlier Office Actions in this application should be directed to Dr. Gary E. Hollinden whose telephone number is 703/308-4521. Dr. Hollinden's office hours are from 6:30 am to 3:00 pm on Monday through Friday.

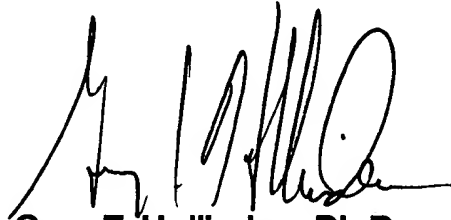
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Reissue of 5,413,774

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Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is 703/308-1235.

A handwritten signature in black ink, appearing to read 'Gary E. Hollinden', is written over the printed name.

Gary E. Hollinden, Ph.D.

Primary Examiner

Group 1600